REMARKS

Applicants respectfully request reconsideration of the present application, in view of the foregoing claim revisions and the following comments.

I. Introduction

Claims 13-15 and 17-24 are pending. Claims 37 and 38 have been added. Support of the amendment can be found in the specification, for example, at page 13, lines 3-9 and at page 14, lines 6-7.

II. Rejection of Claims 13-15 and 17-24 under §101

The examiner has rejected claims 13-15 and 17-24 for the lack of an asserted and credible or a well-established utility. Applicants respectfully traverse this rejection.

THE PTO's BURDEN UNDER SECTION 101 IS SUBSTANTIAL: According to MPEP §2107.02, at page 2100-37, an applicant must advance a credible assertion of a specific utility, thereby to satisfy §101 and §112 in this context, for the claimed invention as a whole. Conversely, to "violate §101, the claimed device must be **totally** inoperable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.,* 977 F.2d 1555, 1571 (Fed. Cir. 1992) (emphasis added). In the same vein:

> "A small degree of utility is sufficient...The claimed invention must be only capable of performing some beneficial function...An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely...A commercial successful product is not required...Nor is it essential that the invention accomplish all its intended functions...or operate under all conditions...partial success being sufficient to demonstrate patentable utility...In short, the defense of non-utility cannot be sustained without proof of total incapacity." If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on a lack of utility is not appropriate. See *In re Brana,* 51 F.3d 1560 (Fed. Cir. 1995); In *re Gardner*, 475 F.2d 1389 (CCPA), *reh'g denied*, 480 F.2d 879 (CCPA 1973); In re *Marzocchi*, 439 F.2d 220 (CCPA 1971).

E. I. du Pont De Nemours and Co. v. Berkley and Co., 620 F.2d 1247, 1260 n17 (8th Cir. 1980) (original emphasis). See also MPEP 2107.01, II, page 2100-33.

CREDIBLE UTILITY OF CO-CULTURE PRODUCTS: The examiner contends that (A) the claims read upon introducing living cancer cells into a subject and yet (B) no credible utility is indicated for administering active tumor cells to a human subject.

At the outset, however, applicants would emphasize that the pending claims are directed to a composition, not to a method of the using the claimed composition. Accordingly, the examiner's stated rationale is founded on an inaccurate interpretation that "the claims read upon introducing living cancer cells into a subject."

Furthermore, there is nothing taught or implicated by the present application that would prompt the knowledgeable reader to implement the claimed invention in the manner identified by the examiner, *i.e.*, by administering active tumor cells to a subject. To the contrary, the examiner correctly notes that applicants' working examples illustrate the use of pre-administration irradiation, which precludes the sort of administration posited by the examiner (see Example 4).

An applicant's assertion of utility is presumed sufficient to satisfy the "utility" requirement. See MPEP 2107.02, III-A, page 2100-40. Against this presumption, the examiner must determine "whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided." MPEP 2107.02, III-B.

Reading the present specification, with knowledge of the toxicity of active tumor cells, a person of ordinary skill surely would understand that, when administered to a subject, the claimed composition cannot include tumor cells in active form. It is the examiner's burden to show the contrary, suing objective evidence that applicants' asserted utility is incredible. Applicants respectfully submit that there is no such evidence of record, which is reason enough for the examiner to withdraw the "lack-of-utility" rejection under Section 101.

"LESS IMMUNOGENIC TUMORS": The examiner further alleges that "there is no credible evidence provided that less immunogenic tumors of humans can be similarly treated, or that the composition can be used against tumors that arose spontaneously

and successfully evaded the immune system to allow them to become established from an initially low tumor burden." Office action at page 3.

In order to rebut a presumption of utility, the examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt or question the truth of the statement of utility by providing the evidence sufficient to present countervailing facts and reasoning. MPEP 2107.02, III-A,. page 2100-40

To sustain his burden of proof in this regard, the examiner is heard to invoke Fenton *et al., J. Nat'l Cancer Inst.* 87(4):241-43 (1995). In particular, the examiner attempts to cast doubt on of the credibility of treating human tumors, in accordance with the present invention, by citing Fenton for the proposition that human tumors are poorly immunogenic.

Yet the Fenton publication also mentions that "several findings in patients during the last 3 years with melanoma have given rise to optimism that at least some tumor types may be susceptible to immune attack" (left column, lines 11-13). Thus, Fenton actually bolsters rather than detracts from the prospect of treating at least some tumor types, pursuant to applicants' teaching.

In the context of speculating on how a clonally heterogeneous mixture of tumor cells escape killing, Fenton *et al.* does suggest that a heterogeneity of class I MHC expression within a tumor-cell population, resulting in antigen-processing defects, may constitute a significant obstacle to antigen-specific T-cell therapy. What the Fenton article questions in this regard, however, is whether *in vivo* administration of interferon gamma may influence class I MHC expression in a proportion of patients.

This emphasis in Fenton, an article published some two years before the priority date of the present application, should not obscure the fact that the present invention takes into account the possibility that, in some instances, mature dendritic cells ("DCs") from a tumor-bearing host have defects in antigen presenting cell ("APC") function, and also that human cancer cell can release soluble factors that can inhibit the maturation of dendritic cells. In light of these potential obstacles, the inventors conceived of using DCs in co-culture with tumor cells, thereby to circumvent the tumor-induced APC dysfunction that, in a somewhat different context, was the focus of Fenton *et al.*

Accordingly, the Fenton publication does not substantiate a reasonable doubt over the stated utility of applicants' claimed invention, ***which itself addresses the concern of Fenton***.

The examiner also questions applicants' stated utility by asserting that test data in the specification are from experiments that employed "highly immunogenic," murine tumor cell lines. Yet, in adjudging whether *in vitro* data or animal tests support an asserted utility, the examiner should gauge whether a skilled person would view the data as reasonably predictive of the asserted utility. MPEP 2107.03, III, page 2100-44.

On this point, applicants would emphasize again that the claimed composition employs DC/tumor-cell co-culture, not tumor cells alone. As explained above, the use of DC not only boosts immunogenecity in DC/tumor-cell co-culture vaccines but also compensates the impact of poor immunogenic tumor cells on inducing immune response.

Moreover, the appended publication of Celluzzi *et al.*, *J. Immunol.* 1998: 1, evidences an understanding in the art that data obtained from murine DC/tumor-cell co-culture vaccines are indicative of the immunotherapeutic effects of human DC/tumor-cell; this, because human DCs are phenotypically and functionally similar to the murine DCs. This understanding also has been validated by human test data published by Kugler *et al.*, *Nature Medicine* 6: 332-336 (2000). More specifically, Kugler *et al.* present a human vaccination study that employed a DC/tumor-cell hybrid, and the authors conclude that hybrid-cell vaccination is effective therapy for human metastatic renal cell carcinoma. See page 332, left column, lines 19-22 and page 335, left column, second full paragraph.

Accordingly, the evidence of record supports the proposition that a person skilled in immunotherapy would accept applicants' murine-model test data as being reasonably predictive of an application humans and, hence, as supporting the credibility of the asserted utility. Conversely, the examiner has not marshaled convincing evidence or explanation as to why a skilled person would disbelieve the utility of the claimed invention, notwithstanding the state of contemporary knowledge after Fenton (1995). Even with Fenton, therefore, the examiner has not sustained his burden to rebut the

presumption of credibility that attaches to applicants' teaching of utility for the claimed invention.

III. ***Rejection of claims 13-15 and 17-24 under 35 USC §112, first paragraph***

The examiner also has rejected claims 13-15 and 17-24, asserting lack of enabling disclosure. The rationale for this "non-enablement" rejection under Section 112 appears to be the same as that for the above-discussed "lack of utility" rejection under Section 101. Because the latter rejection is ill-conceived, for the reasons detailed above, applicants submit that the accompanying non-enablement rejection likewise should not be maintained. Accordingly, reconsideration and withdrawal of both rejections are requested.

In view of the foregoing amendment and remarks, applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The examiner is invited to contact the undersigned by telephone, should he feel that any other issue requires consideration.

Respectfully submitted,

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